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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/752,342	01/06/2004	Graham Michael Wynne	OS-10001	4508

38724 7590 12/30/2004

OSI PHARMACEUTICALS, INC.
58 SOUTH SERVICE ROAD
MELVILLE, NY 11747

EXAMINER	
LEE, SUSANNAH E	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 12/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/752,342	WYNNE ET AL.	
	Examiner	Art Unit	
	Susannah Lee	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *15-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/1/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 22-39 have been canceled by amendment filed on 11/01/2004. Claims 1-21 are pending in this application.

Information Disclosure Statement

Applicant's information disclosure statement (IDS), filed on 11/01/2004 has been considered. Please refer to Applicant's copies of the 1449 submitted herewith.

Priority

This application claims benefit of Provisional Application No. 60/438,152, filed on 01/06/2003, which a patent has not been issued as of 11/30/2004. This application names an inventor or inventors named in the prior application.

Response to Election/Restrictions

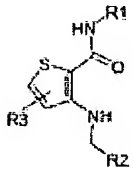
Claims 15-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected compounds and methods, there being no allowable generic or linking claim. Claims 15-21, drawn to methods of use of compounds of Claims 1-14 may be rejoined according to M.P.E.P. §821.04 should the compounds of Group I be found allowable. Election was made **without** traverse in a reply filed on 01 November 2004 and in a telephone call made to Attorney Shu Lee on 17 November 2004.

Status of the Claims

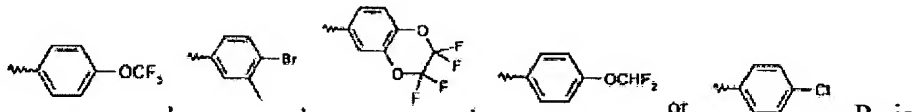
Claims 1-21 are pending in this application. Claims 15-21 are withdrawn from further consideration by the examiner, 37 C.F.R. §1.142(b), as being drawn to a non-elected invention. The withdrawn subject matter is patentably distinct from the elected subject matter as it differs in

structure and element and would require separate search considerations. In addition, a reference, which anticipates one group, would not render obvious the other.

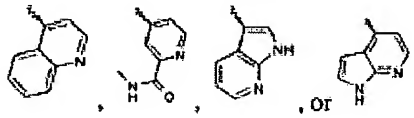
The scope of the invention of the elected subject matter is as follows:



Compounds of formula (I), (I) , depicted in claim 1, wherein: R_1 is



; R_2 is



, and R_3 is C_{0-4} alkyl.

Claims 15-21 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 11-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As stated in the MPEP 2164.01(a), "there are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue."

In In re Wands, 8 USPQ 2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described. They are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the amount of direction or guidance present,
5. the presence or absence of working examples,
6. the breadth of the claims,
7. the quantity of experimentation needed, and
8. the level of the skill in the art.

In the instant case,

The nature of the invention

The nature of the invention of claim 11-13 is an anti-neoplastic, anti-tumor, anti-angiogenic, chemotherapeutic, cytotoxic cancer therapeutic, or angiogenesis inhibiting cancer therapeutic agent of compound of formula (I). Page 1 of the specification discloses that the present invention is directed to (2-carboxamido)(3-amino)thiophenes that are inhibitors of c-Kit proto-oncogene, which is believed to be important in the treatment of tumors.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening in vitro and in vivo to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instant claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to therapeutic effects of the above listed diseases, whether or not the disease is effected by the inhibition of c-Kit proto-oncogene would make a difference.

Applicants are claiming a method of treating anti-cancer diseases, which includes anti-neoplastic and anti-tumor, by administering a compound of the formula (I). The state of the prior art is that cancer therapy remains highly unpredictable. The various types of cancers have different causative agents, involve different cellular mechanism, and consequently, differ in treatment protocol. It is known that the challenge of cancer treatment has been to target specific therapies to pathogenetically distinct tumor types, that cancer classification has been based primarily on morphological appearance of the tumor and that tumors with similar

histopathological appearance can follow significantly different clinical courses and show different responses to therapy (Golub et al. page 531). Furthermore, it is known that chemotherapy is most effective against tumors with rapidly dividing cells and that cells of solid tumors divide relatively slowly and chemotherapy is often less effective against them. It is also known in the prior art that the role of NO in tumor biology remains incompletely understood with both the promotion and inhibition of NO mentioned for the treatment of tumor progression and only certain human cancers may be treated by selected NO-blocking drugs (Lala et al. page 91). These examples show that there are different cellular mechanisms, the unpredictability in the art and the different treatment protocols.

Hence, in the absence of a showing of correlation between all the diseases claimed as capable of treatment by the inhibition of c-Kit proto-oncogene, one of skill in the art is unable to fully predict possible results from the administration of the compound of the claims. This is due to the unpredictability of the role of the inhibition of c-Kit proto-oncogene. Also, various types of cancers have different causative agents, different cellular mechanisms, and differ in treatment protocol.

The amount of direction or guidance present and the present of absence of working examples

The only direction or guidance present in the instant specification is the listing of diseases applicant considers as anti-cancer agents associated with c-Kit proto-oncogene activity, pages 1-3 of the specification. There are no working examples present for the treatment of anti-cancer. Applicants are invited to point out where in the original application a working example is present.

The breadth of the claims

The breadth of the claims is the treatment of any cancer with any compound of formula (I). Cancer disorders, include, for example, as found on page 2 of the instant specification, breast cancer, head and neck cancer, gastrointestinal cancer, leukemia, ovarian, and lung cancer.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases out of all diseases would be benefited (treated) by the inhibition of c-Kit proto-oncogene and would furthermore then have to determine which of the claimed compounds would provide treatment of which disease, if any.

The level of the skill in the art

The level of the skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the compound of the instant claims for the treatment of any cancer. As a result necessitating one of skill to perform an exhaustive search for which diseases can be treated by what compounds of the instant claims in order to practice the claimed invention.

Genentech Inc. v. Novo Nordisk A/S, (CAFC) 42 USPQ 2d 1001, states that a "patent is not a hunting license. It is not a reward for search, but compensation for its successful

conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Therefore, in view of the Wands factors and In re Fisher discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test which diseases can be treated by the compound encompassed in the instant claims, with no assurance of success.

This rejection can be overcome by deleting the claims.

Claim Rejections - 35 USC § 103

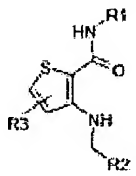
The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

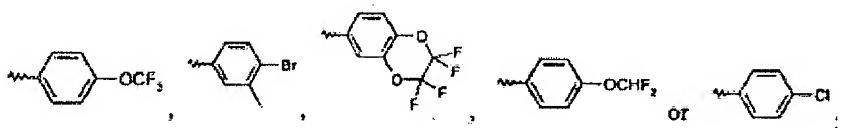
The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

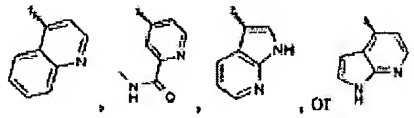
Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wood et al., U.S. Pat. No. 6,187,799.



Applicants instant elected invention teaches the compound of formula, (I) , depicted in claim 1, their pharmaceutically acceptable salts or N-oxides wherein: R_1 is

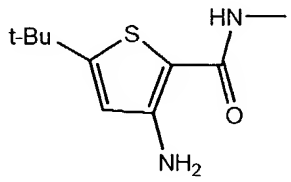


, R_2 is



, and R_3 is C_{0-4} alkyl. These products are used as anti-cancer agents.

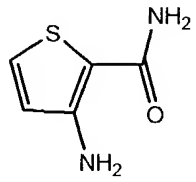
Determination of the scope and content of the prior art (MPEP § 2141.01)

Wood teaches thiophene compounds of formula,  , 3-amino-5-(1,1-dimethylethyl)-N-methyl-2-thiophenecarboxamide, CAS RN 216574-52-6, and the pharmaceutically acceptable salt or N-oxide. (See US 6,187,799 and STN search notes). These products can be used for the treatment of cancerous cell growth (Claim 1, lines 65-66).

Ascertainment of the difference between the prior art and the claims (MPEP § 2141.02)

The difference between the prior art of Wood and the claims is that in the instant application there is a substituted benzyl group instead of a methylamino group and the amino group is substituted with a methyl pyridine functional group at 3 position instead of an unsubstituted amino group.

Finding of prima facie obviousness – rationale and motivation (MPEP § 2142-2413)

One skilled in the art would have found the claimed compound prima facie obvious because the instantly claimed compound and the compound in Wood have the same core structure, 

, 3-aminothiophene-2-carboxamide. The motivation to make the claimed compounds derives from the expectation that structurally similar compounds would possess similar activity (i.e. pharmacological use). Both the instantly claimed compounds and the compounds of Wood are used for the treatment of cancer. Although, applicant's compound differs in the addition of some functional groups from the prior art, they are used for the same pharmacological use so one skilled in the art would expect the species would have similar properties as the genus.

Conclusion

Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wood et al., U.S. Pat. No. 6,187,799 at this point in the examination process. Claims 11-13 are rejected under 35 U.S.C. 112, first paragraph as failing to comply with the enablement requirement.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susannah Lee whose telephone number is (571) 272-6098. The examiner can normally be reached on M-F, 8am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susannah Lee
Patent Examiner, AU 1626

for Kamal Saeed
Joseph K. McKane
Supervisory Patent Examiner
AU 1626
Date: 12/15/04